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MAIL STOP - PCT
Attorney Docket No.: 27319U
Date: 10 July 2006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Art Unit: Unknown

HESSLINGER, et al.

Examiner: Unknown

Appl. No.: 10/576,712

Filed: April 21, 2006

Intl. Application No.: PCT/EP2004/052725

Intl. Filing Date: October 29, 2004

Title: **USE OF BH4 FOR THE TREATMENT OF RESPIRATORY DISEASES**

TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Submitted herewith for filing in the U.S. Patent and Trademark Office is the following:

- 1) Supplemental Information Disclosure Statement;
- 2) Supplemental PTO Form-1449 with 17 references cited, with copies of 14 of the 17 references.

The Commissioner is hereby authorized to charge any deficiency or credit any excess to Deposit Account No. 14-0112.

Respectfully submitted,
NATH & ASSOCIATES PLLC

By: _____

Gary M. Nath
Reg. No.: 26,965
Sheldon M. McGee
Reg. No.: 50,454
Customer No.: 34375

SMM/1e



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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

An Information Disclosure Statement is submitted herewith pursuant to 37 C.F.R. 1.97-1.98. Please note the following particulars: [NOTE: One only of items a, b, c, and d must be checked.]

a. ☒ [XXX] The enclosed statement is being filed within three months of the filing date of a national application, or within three months of the date of entry into the national stage as set forth in 37 C.F.R. 1.491 in an international application, or before the mailing date of a first Office Action on the merits, whichever event occurs last.

b. ☐ [] The enclosed statement is being filed after a first action on the merits but before the mailing date of a final action under 37 C.F.R. 1.113, or a notice of allowance under 37 C.F.R. 1.311.

The enclosed statement is accompanied by [check one]:

- ☐ i. a certification in part (e) below as specified in 37 C.F.R. 1.97(e), or
- ☐ ii. a check in the amount required by 37 C.F.R. 1.17(p).

- c. ☐ The enclosed statement is being filed after the mailing date of a final action under 37 C.F.R. 1.113, or a notice of allowance under 37 C.F.R. 1.311, but before payment of the issue fee.
☐ Certification report(e) below; and
☐ a check in the amount as required by 1.17(p).
- d. ☐ The enclosed statement is being filed pursuant to 37 C.F.R. 1.97(i), for placement in the file.
- e. Certification [Check one] [Certification is required only if box (b)(i) or box (c) is checked.]
- ☐ I hereby certify that each item of information contained in the enclosed Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement,
or
- ☐ I hereby certify that no item of information in the enclosed Information Disclosure Statement herewith was cited in a communication from a foreign patent office in a counterpart foreign application, or, to my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.
or
- ☐ Appropriate certification is attached.
- f. [XXX] If no check is enclosed and a fee is due in connection with this communication or if the check enclosed is insufficient, the Commissioner is authorized to charge any fee or additional fee due in connection with this communication to Deposit Account No. 14-0112.
- g. [XXX] Copies of the documents are attached herewith with a completed Form PTO-1449.

[] Copies of the documents are not attached as
allowed under CFR 1.98(d)(1)(2). The earlier
application is identified as:

and / or

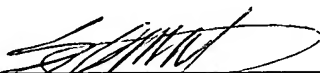
[XXX] Copies of US Patents/Publications not attached, with
a completed Form PTO-1449, as allowed in Official
Gazette Aug. 5, 2003/ Vol. 1273, no. 1.

The Examiner is respectfully requested to cite the
documents listed on the attached Form PTO-1449 in the next
Office Action. In so doing, the Examiner is respectfully
requested to initial in the space adjacent to the listing of
each document on the Form PTO-1449, and return a copy of the
initialed Form PTO-1449 with the next communication to
Applicants, to confirm that these documents have been considered
by the Examiner and made of record in this application.

If the Examiner has any questions or wishes to discuss this
application, kindly telephone the undersigned at the below-
listed number.

Respectfully submitted,
NATH & ASSOCIATES PLLC

By:



Gary M. Nath
Reg. No.: 26,965
Sheldon M. McGee
Reg. No.: 50,454
Customer No.: 34375

SMM/le

JUL 10 2006

(SUPPLEMENTAL)

Attorney Docket No.: 27319U

FORM PTO-1025
INFORMATION DISCLOSURE CITATION

In re Application of:
HESSLINGER, et al.

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Filed:
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Art Unit:
Unknown

Examiner:
Unknown

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Issue / Publication Date	Inventor	Filed
A1	2002/0052374 A1	2 May 2002	Rabelink et al.	7 June 2000
A2	5,877,176	2 March 1999	Gross	15 November 1993
A3	5,830,461	3 November 1998	Billiar et al.	8 November 1996

FOREIGN PATENT DOCUMENTS

Examiner Initial	Document Number	Publication Date	Country	Translation
A4	0 079 574 B1	25 May 1983	EP	N/A
A5	00/21509 A2	20 April 2000	WO	N/A
A6	98/35055 A1	13 August 1998	WO	N/A

OTHER

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A7	Guzik, T.J., et al., "Mechanisms of Increased Vascular Superoxide Production in Human Diabetes Mellitus: Role of NAD(P)H Oxidase and Endothelial Nitric Oxide Synthase", <u>Circulation</u> , Vol. 105, Pps. 1656-1662, (2002).
A8	Katusic, Z.S., "Vascular endothelial dysfunction: does tetrahydrobiopterin play a role?", <u>Am J Physiol Heart Circ Physiol</u> , Vol. 281, Pps. H981-H986, (2001).
A9	Marinos, R.S., et al., "Tetrahydrobiopterin levels regulate endothelial cell proliferation", <u>Am J Physiol Heart Circ Physiol</u> , Vol. 281, Pps. H482-H489, (2001).
A10	Meininger, C.J., et al., "Impaired nitric oxide production in coronary endothelial cells of the spontaneously diabetic BB rat is due to tetrahydrobiopterin deficiency", <u>Biochem. J.</u> , Vol. 349, Pps. 353-356, (2000).
A11	Shinozaki, K., et al., "Oral Administration of Tetrahydrobiopterin Prevents Endothelial Dysfunction and Vascular Oxidative Stress in the Aortas of Insulin-Resistant Rats", <u>Circ Res.</u> , Vol. 87, Pp. 566-573, (2000).
A12	Shinozaki, K., et al., "Abnormal Biopterin Metabolism is a Major Cause of Impaired Endothelium-Dependent Relaxation Through Nitric Oxide/O ₂ ⁻ Imbalance in Insulin-Resistant Rat Aorta", <u>Diabetes.</u> , Vol. 48, Pp. 2437-2445, (1999).
A13	Sumi-Ichinose, C., et al., "Catecholamines and Serotonin are Differently Regulated by Tetrahydrobiopterin", <u>The Journal of Biological Chemistry</u> , Vol. 276, No. 44, Pps. 41150-41160, (2001).
A14	Thöny, B., et al., "Tetrahydrobiopterin biosynthesis, regeneration and functions", <u>Biochem. J.</u> , Vol. 347, Pps. 1-16, (2000).
A15	Tiefenbacher, C.P., "Tetrahydrobiopterin: a critical cofactor for eNOS and a strategy in the treatment of endothelial dysfunction?", <u>Am J Physiol Heart Circ Physiol</u> , Vol. 280, Pps. H2484-H2488, (2001).
A16	Walter, R., et al., "Inhalation of the Nitric Oxide Synthase Cofactor Tetrahydrobiopterin in Healthy Volunteers", <u>Am J Respir Crit Care Med</u> , Vol. 156, Pps. 2006-2010, (1997).
A17	Wei, C., et al., "Why do nitric oxide synthases use tetrahydrobiopterin?", <u>Journal of Inorganic Biochemistry</u> , Vol. 91, Pps. 618-624, (2002).

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP ' 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.